## REMARKS

Claims 1, 3, 5-7, 9-19, 21, 23-25 and 27-35 are pending. Claims 1, 3, 5-7, 9-19, 21, 23-25 and 27-35 have been cancelled. Claims 36-53 are newly added. An Appendix of Pending Claims is attached for the Examiner's convenience.

Support for new claim 36 is found in Figures 1A and 1B and the Brief Description of the Drawings found at page 2, lines 4-10. Figure 1A and 1B depict a solid support member **5**, a sample handling well **40**, a sample inlet port **10**, a first microchannel **15** a detection module **30**, a detection electrode **35**, and a second microchannel **15, 20A, or 20B** extending between the sample handling well **40** and the detection module **30**. Moreover, the basic system of wells and microchannels described in claim 36 are well known to those of skill in the art and are referred to as mesoscale flow systems (see U.S. Patent 5,304,487, column 1 through 2, attached as Exhibit 1). Thus, Applicants submit the features recited in claim 36 are supported by Figures 1A and 1B and the Brief Description of the Drawings found at page 2, lines 4-10.

Support for new claims 37-39 is found at page 11, line 4-30 of the specification. Specifically, the specification discusses the inclusion of a cell handling module that can be used for a number of different purposes depending on the reagents or materials positioned within the cell handling module (see page 11, lines 16-29). As recited in claims 37 and 38, reagents commonly used for cell lysis can be positioned within the cell handling module (see specification at page 11, lines 24-26). As recited in claim 39, removal of cellular debris following cell lysis can be accomplished via the addition of a filter adapted for the removal of cellular debris (see specification at page 11, lines 30-33). Moreover, U.S. Patent 5,304,487, incorporated by reference at page 8, line 21, describes a filter adapted for such purpose (column 6, lines 52-54). As set forth in the M.P.E.P. § 608.01(p), it is permissible to incorporate essential material, i.e., material that supports the claims, known to those of skill in the art if the material is a U.S. Patent. Accordingly, Applicants submit that the features recited in claims 37-39 are supported by the specification and U.S. Patent 5, 304,487 (attached as Exhibit 1).

Support for new claims 40 and 41 is found in the specification at page 12, lines 1-12 and in U.S. Patent 5,304,487. Specifically, as outline at page 12, lines 1-12 the cell handling module includes a cell a cell separation or capture module. This embodiment utilizes a cell capture region comprising binding sites capable of binding a molecule of interest. As recited

in claim 41, the cell capture region may comprise binding moieties for the capture of a cell molecule attached to beads. See also column 6, line 62 through column 7, line 5 of U.S. Patent No. 5,304,487.

Support for new claims 42-44 is found in the specification at page 12, line1, page 14, line 31 through page 15, line 31, U.S. Patents 5,770,029, 5,126,022, 5,631,337, 5, 569,364, 5,750,015, and 5,135,627; all of which were incorporated by reference. Accordingly, Applicants submit that the features recited in claims 37-39 are supported by the specification and U.S. Patents 5,770,029, 5,126, 022, 5,631,337, 5, 569,364, 5,750,015 and 5,135,627. Copies of these Patents are attached hereto as Exhibits 2-7.

Support for new claims 45-46 is found in Figure 1D, the specification at page 2, lines 12-15, and page 15, line 32, through page 17, line 10. Specifically, Figure 1D depicts a reaction module **45**, positioned between a sample handling well **40** and a detection module **30**. As shown in Figure 1D, the reaction module is in fluid communication with the sample handling well and the detection module via microchannels. Accordingly, Applicants submit that the features recited in claim 45 are supported by Figure 1D.

Specific uses for the reaction module are set forth in the specification at page 15, line 32, through page 17, line 10. Beginning at page 16, line 31, the reaction module may be used for the biological alteration of the sample. As recited in claim 46, one such alteration includes nucleic acid amplification. Amplification is accomplished by the positioning the required reagents in the reaction module. As the reagents and techniques for the amplification of nucleic acid is well known to those of skill in the art, Applicants submit that claim 46 is supported by the specification.

Support for new claims 47 and 48 is found in the specification at page 38, lines 24-31 and U.S. Patent Nos. 5,498,392 and 5,587,128, describing the use of heaters in microfluidic devices (attached hereto as Exhibits 8 and 9). Accordingly, Applicants submit that claims 47 and 48 are supported by the specification.

Support for new claims 49-50 is found in the specification at page 39, line 11 through page 41, line 4 and U.S. Patent 5,304,487, column 9, 34-48, describing the use of a pump as a means for providing sufficient flow through the system. Accordingly, Applicants submit that claims 59 and 50 are supported by the specification.

Support for new claims 51-52 is found in the specification at page 41, line 5-13 and in U.S. Patent 5, 304,487, column 10, lines 13-25, describing the use of valves for control the flow of fluid through the system. Accordingly, Applicants submit that claims 51 and 52 are supported by the specification.

Support for new claim 53 is found in the specification at page 14, lines 3-7. Accordingly, Applicants submit that claim 53 is supported by the specification.

Drawings

The drawings have been objected to under 37 CFR §1.83(a) for failing to show every feature specified in the claims. Further, the proposed additional sheets of drawings filed on June 19, 2001 have been disapproved because they introduce new matter into the disclosure of the specification. Claims 1, 3, 5-7, 9-19, 21, 23-25 and 27-35 have been cancelled. Moreover, as outlined above, the drawings, support the features recited in newly added Claims 27-35. Accordingly, Applicants respectfully request that the rejection based on the drawings be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-18 and 23-35 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Claims 1-18 and 23-35 have been cancelled. Accordingly, Applicants request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1, 3, 5-7, 9-19, 21, 23-25 and 27-35 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Claims 1, 3, 5-7, 9-19, 21, 23-25 and 27-35 have been cancelled. Accordingly, Applicants request withdrawal of the rejection.

Attached hereto is a marked-up version of the changes made to the claims by the "Restriction and Amendment". The attached page is captioned **"Version with markings to show changes made."**

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Dated: 3/11/02

Respectfully submitted,

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## "VERSION WITH MARKINGS TO SHOW CHANGES MADE"

Claims 1, 3, 5-7, 9-17,19, 21, 23-25, and 27-35 have been cancelled.

Appendix of Pending Claims

36. A microfluidic device for the detection of a target analyte in a fluid sample comprising:
a) a solid support member;
b) a sample handling module including a sample handling well formed in said support member to receive and store said sample;
c) a sample inlet port to said microfluidic device;
d) a first microchannel formed in said support member and fluid coupled to and extending between said sample handling well and said sample inlet port;
e) a detection module including a detection well formed in said support member and a detection electrode positioned in said detection well, said detection electrode being provided with a self-assembled monolayer and a binding ligand; and,
f) a second microchannel formed in said support member and extending between said sample handling well and said detection well for the flow of said fluid sample there between.

37. The device of claim 36, and a reagent positioned in said sample handling well.

38. The device of claim 37 wherein said reagent comprises a cell lysing agent.

39. The device of claim 36, and a filter adapted for the removal of cellular debris, said filter positioned between said sample handling well and said second microchannel.

40. The device of claim 36, and a cell capture structure provided in said sample handling well.

41. The device of claim 40 wherein said cell capture structure comprises binding moieties immobilized on the surface of beads.

42. The device of claim 36, and a cell separation structure provided in said sample handling well.

43. The device of claim 42 wherein said cell separation structure comprises an electrophoretic microchannel and electrodes.

44. The device of claim 43 wherein said cell separation structure further comprises electrophoretic gel media.

45. A device according to claim 36, and a reaction module including a reaction well formed in said support member, wherein an additional microchannel connects the reaction module to said sample handling module and a further microchannel connect the reaction module to said detection module.

46. A device according to claim 45, and reagents for nucleic acid amplification positioned in said reaction module.

47. A device according to claim 45, and an electrical resistance heater positioned in said reaction module.

48. A device according to claim 36, and an electrical resistance heater positioned in said sample handling module.

49. A device according to claim 36, and a means for inducing flow of a sample through said microfluidic device.

50. A device according to claim 48 wherein said means for inducing flow comprises a pump.

51. A device according to claim 36, and a means for holding said sample.

52. A device according to claim 50 wherein said means for holding said sample is a valve means disposed of within said microfluidic device.

53. A device according to claim 36 wherein said binding ligand is a nucleic acid.